

**REMARKS**

Applicants thank the Examiner for her courtesy during the August 30, 2007 telephone interview and, as discussed, submit this supplemental response and amendment to correct the August 20, 2007 amendments to claims 1, 9, 14 and 15. Claims 1, 14 and 15 should have been amended to recite “insoluble particles” for steps (b) and (c) not “paramagnetic complex”. Applicants have therefore amended claim 1, 14 and 15 to recite “insoluble particles” as shown above. Applicants have also amended claim 9 to correct the grammar.

Applicants also restate their prior remarks from August 20, 2007, and have revised them to refer to the claim as currently amended. Applicants remarks follow:

Claims 1-13 were pending in this application. Claims 1-13 were previously amended in the August 20 response and amendment to recite methods of cellular labeling. Additionally, new claims 14 and 15 were previously added in the August 20 response and amendment. Thus, claims 1-15 are currently pending in this application.

Applicants thank the Examiner for her courtesy during the most recent telephone interview and note the agreement to consider amending the presently pending claims to method claims provided they do not cause a restriction. Applicants have therefore amended the claims to methods in line with the Examiner’s comments.

Support for the amendments and new claims can be found throughout the specification, drawings and original claims as filed. For example, support for the amendments to claims 1-13 can be found in the original claims as filed, as well as in the specification at p. 4, lns 7-12, p. 5 lns 11-14 and 17-20, p. 6 lns. 6-8 and p. 7 ln 1. Support for claim 14 can be found at, for example, p. 6 lns. 18-20 of the specification. Support for claim 15 can be found, for example,

at p. 2 lns 23-24 of the specification. Therefore no new matter has been added by these new claims and claim amendments.

Additionally, the specification has been amended to add a Brief Description of the Drawings. In addition to the figures themselves, support for this amendment can be found in the text of the specification at, for example, p. 8 (for Figs. 1 and 2), p. 9 (for Figs 3 and 4), p. 10 (for Fig. 5), p. 1 (for Fig. 6) and pp. 5-7 (for Fig. 7). Therefore no new matter has been added by the amendment to the specification.

### **Objections to the Specification**

The specification has been objected to because it lacks a “Brief Description of the Drawings” section. As discussed above, applicants have amended the specification to add the aforementioned section. Withdrawal of the objection to the specification is therefore requested.

### **35 U.S.C. § 102**

Claims 1, 4, 6, and 8-10 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Tokumitsu et al., STP Pharma Sciences, 2000, 10(1), p. 39-49 (“Tokumitsu”). Additionally, claims 1, 4-7 and 9-13 have been rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Pat. No. 5,155,215 (“Ranney”). Lastly, claims 1-3 and 6 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Kabalka et al., Magnetic Res. in Med., 1988, 8, p. 89-95 (“Kabalka”).

At the outset, applicants note that in order to anticipate a claim, a reference must disclose or teach each and every limitation of the claims. Applicants respectfully traverse the § 102(b) rejections because each of the above-cited references do not disclose or teach each and every limitation of the claims.

Applicants note the Examiner's statement that certain elements of the claims were not considered because the claims were directed to products, not methods. As discussed above, the claims have been amended to recite methods. Therefore, consideration of all of the elements of the claims is requested.

Exemplary amended independent claim 1 reads as follows:

A method of cellular labeling comprising the steps of:  
(a) exposing insoluble particles comprising at least one paramagnetic complex of lanthanide or transition metal chelates to cells;  
(b) internalizing the insoluble particles inside the cells and  
(c) degrading the insoluble particles by enzymes or by effectors in the environment surrounding the insoluble particles to form water soluble MR-imaging probes.

Applicants note that none of Tokumitsu, Ranney or Kabalka discloses or teaches a cellular labeling method. Furthermore, none of the aforementioned references disclose or teach exposing insoluble particles comprising at least one paramagnetic complex of lanthanide or transition metal chelates to cells and internalizing the insoluble particles inside cells.

In contrast, Tokumitsu describes gadolinium-loaded chitosan particulate devices (as micro- and nano- particles) which have a prolonged retention in tumor tissues after intratumoral injections in gadolinium Neutron-Capture Therapy trials.

With regard to Ranney, it merely describes an imaging-enhancing agent comprising a biodegradable water-soluble polymer (or microsphere) entrapping a paramagnetic chelated complex conjugated to the polymer. (Ranney at pp. 15, ln. 34 - 16, ln 10 and p. 18, lns. 16-23). Furthermore, Rannney merely describes these compounds as enhancing agents for MRI, especially of blood flow.

Lastly, Kabalka merely describes to paramagnetic liposomal contrast agents for use as MRI contrast agents, especially for imaging the liver.

Thus, applicants submit that, for the above reasons, the presently pending claims are not anticipated by any of Tokumitsu, Ranney or Kabalka. Withdrawal of the § 102(b) rejections is respectfully requested.

### Conclusion

Therefore, for the above reasons, applicants submit that the presently pending claims are in condition for allowance and request the speedy issuance of a notice of allowability.

No fee, except the fee for a one month extension of time, is believed to be due for the filing of this *Amendment and Response to Office Action*. However, the Director is hereby authorized to charge any required fees and credit any overpayments to Deposit Account No. 50-0540.

Respectfully submitted,

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